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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/910,588	07/20/2001	David C. Klein		3159

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NATIONAL INSTITUTE OF HEALTH
C/O Ballard Spahr Andrews & Ingersoll, LLP
SUITE 1000
999 PEACHTREE STREET
ATLANTA, GA 30309

EXAMINER	
FALK, ANNE MARIE	

ART UNIT	PAPER NUMBER
1632	

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03/18/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/910,588	KLEIN ET AL.	
	Examiner	Art Unit	
	Anne-Marie Falk, Ph.D.	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 December 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3, 5-8, 10, 11, 15-17, 19, and 20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *11* is/are allowed.

6)☒ Claim(s) *1-3,5-8,10,15-17,19 and 20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *20 July 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The response filed December 11, 2006 has been entered. No amendments have been made. The revised listing of claims is acknowledged.

The remarks filed December 5, 2005 (hereinafter referred to as "the response") are considered herein. Exhibits 1 and 2, filed December 5, 2005, are acknowledged.

Claims 1-3, 5-8, 10, 11, 15-17, 19, and 20 remain pending in the instant application.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114 was filed in this application after appeal to the Board of Patent Appeals and Interferences, but prior to a decision on the appeal. Since this application is eligible for continued examination under 37 CFR 1.114 and the fee set forth in 37 CFR 1.17(e) has been timely paid, the appeal has been withdrawn pursuant to 37 CFR 1.114 and prosecution in this application has been reopened pursuant to 37 CFR 1.114. Applicant's submissions filed on December 5, 2005 and December 11, 2006 have been entered.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3, 5-8, and 10 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for (i) *in vitro* applications of the claimed methods, wherein an N-bromoacetylated acetyl acceptor substrate or an N-chloroacetylated acetyl acceptor substrate is introduced into a cell expressing an acetyltransferase and (ii) a method of inhibiting melatonin production in a cell

which produces melatonin, as set forth in Claim 11, does not reasonably provide enablement for *in vivo* applications of the claimed methods. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The claims are directed to a method of producing a bisubstrate inhibitor in a cell, a method of inhibiting the activity of an acetyltransferase in a cell, and a method of inhibiting melatonin production in a cell. The claims read on both *in vivo* and *in vitro* applications of the methods.

In view of the data presented in the Declarations of Dr. David Klein filed May 8, 2000 and January 8, 2001, the scope of enablement has been expanded to include any acetyltransferase and additional substrates as recited in the present claims.

As noted at page 4 of the Office Action of October 2, 2002, the specification fails to provide an enabling disclosure for the full scope of *in vivo* applications of the claimed methods because the *in vivo* effects of the various compounds recited in the claims are unknown. No guidance is offered regarding the *in vivo* effect of introducing an acetyltransferase inhibitor into a cell. The specification does not offer any guidance for the manner of using any of the compounds such as those recited in the claims *in vivo*. The specification does not offer any working examples to demonstrate *in vivo* applications of the claimed methods. The specification teaches that the only use for the *in vivo* applications is to provide therapeutic benefit, to limit adverse effects of certain drugs, or to improve the efficacy of certain drugs. However, the specification does not teach how to use the claimed methods to achieve any of these effects. Furthermore, no guidance is provided with regard to how the compounds would be administered or how often the compounds should be administered to produce the desired therapeutic effect. Moreover, the specificity of the inhibitor is essential for the *in vivo* operability of the claimed methods, yet the specification does not offer any guidance regarding the specificity of the inhibitors to be used in the claimed methods. Further lacking is an assessment of the toxicity of the compounds contemplated for use *in vivo*. In the absence of

specific guidance, one skilled in the art would have been required to engage in undue experimentation to practice the claimed methods *in vivo*.

At page 5 of the response, Applicants assert that a well-established utility is recited in the application as filed, the steps for achieving this utility are taught in the application, and the recited utility is validated by data. Applicants assert in particular that a well-established utility taught in the application is the treatment of depression. Applicants point out that the *in vivo* data presented show reduction in melatonin levels, but do not directly show an increase in serotonin in the brain. However, Applicants argue that based on the well-known relationship of serotonin as a precursor of melatonin, one would conclude that reducing melatonin production by the disclosed and exemplified mechanism necessarily indicates increased levels of serotonin because the methods used block the activity of an enzyme that converts serotonin to a precursor of melatonin. Applicants conclude that the present methods therefore increase serotonin in the brain.

At pages 5-6 of the response, Applicants go on to argue that it is well established that decreased serotonin causes depression and it is equally accepted that increasing serotonin treats depression. Applicants allege that there is no objective reason to doubt that increasing serotonin in the brain would treat depression. Applicants go on to say that the application teaches the steps for increasing serotonin in the brain to treat depression and that a patient diagnosed with depression can be treated by administration of an alkylating derivative of an acetyl acceptor substrate of AANAT. Applicants further note that the effectiveness of an alkylating derivative of an acetyl acceptor substrate of AANAT at increasing serotonin in the prescribed dosage range is confirmed in Exhibit C to the response filed January 2, 2003. Applicants are reminded that Exhibit C is not of record and has not been considered (see page 5 of the Office action of 11/29/04). The Examiner cannot comment on evidence that is not of record. Applicants conclude that undue experimentation would not be required to treat depression and that there is no basis

to doubt the role of serotonin in depression or the ability of the steps taught to increase serotonin levels in the brain.

Given Applicants' arguments, it is agreed that administration of an alkylating derivative of an acetyl acceptor substrate of AANAT could be used to increase serotonin levels in the brain and thereby treat depression. However, Applicants' arguments are not commensurate in scope with the scope of the claims, which are directed to inhibiting **any** acetlytransferase and producing **any** treatment effect, including treatment effects that go beyond treating depression. Applicants' arguments pertain only to increasing serotonin levels to treat depression. As such, the arguments pertain only to Claim 11 which is directed to inhibiting melatonin production in a cell which produces melatonin by inhibiting AANAT. Claim 11 is indicated as allowable.

Claims 15-17, 19, and 20 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated cell comprising a bisubstrate inhibitor, wherein the bisubstrate inhibitor is synthesized from an N-bromoacetylated acetyl acceptor substrate or an N-chloroacetylated acetyl acceptor substrate for an acetyltransferase present in the cell and CoA, does not reasonably provide enablement for a cell residing *in vivo*. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

No arguments were presented to address this rejection. The arguments relating to the *in vivo* aspect of the above rejection, presented at pages 5-7 of the response, have already been addressed herein above.

Thus, the rejection under 35 U.S.C. 112, first paragraph, is maintained.

Conclusion

Claim 11 is allowable.

All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet.

The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne-Marie Falk whose telephone number is (571) 272-0728. The examiner can normally be reached Monday through Friday from 9:00 AM to 5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras, can be reached on (571) 272-4517. The central official fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Anne-Marie Falk, Ph.D.

/Anne-Marie Falk/
Primary Examiner, Art Unit 1632